CLAIMS

1. An array of at least two different oligodeoxyribonucleotide probes, containing a sequence capable of forming a specific duplex with a target polynucleotide, or one of its variants, characterized in that said array consists of or comprises a set of distinct probes for detecting and/or quantifying, in a sample, the potential presence of any target oligonucleotide derived from an mRNA fragment encoding a membrane receptor from a mammalian cell, which may comprise at least one editing site in the sequence of this fragment, and in that at least one of the nucleotides dG on at least one of said probes has been substituted with a nucleotide dI, such that the hybridization conditions are identical for each of said probes.

2. The array of at least two different probes as claimed in claim 1, characterized in that the number and the location of the substitutions of nucleotide dG with a nucleotide dI in said probes are determined such that the Tm values of the duplexes which may be formed with each of said probes are identical or sufficiently close to make it possible to obtain said duplexes by specific hybridization under the same hybridization conditions for each of said probes.

3. The array of at least two different probes as claimed in either of claims 1 and 2, characterized in that the number and the location of the substitutions of nucleotide dG with a nucleotide dI on said probes are determined such that the number of remaining dGs capable of pairing with dC or with C in said duplexes is identical or hardly different for each of said probes.

4. The array of at least two different probes as claimed in one of claims 1 to 3, characterized in that said probes are of the single-stranded DNA type.

5. The array of at least two different probes as claimed in one of claims 1 to 4, characterized in that said probes comprise a small number of bases, preferably equal to or less than 20 bases.

6. The array of at least two different probes as claimed in one of claims 1 to 5, characterized in that said probes use an identical number of bases or a number of bases that differs at most by 10%.

7. The array of at least two different probes as claimed in one of claims 1 to 6, characterized in that the number of said different probes is at least equal to the number of expected variants of said target polynucleotide, at least one of which is liable to be present in said sample to be analyzed.

8. The array of at least two different probes as claimed in one of claims 1 to 7, characterized in that the number of said probes in which at least one of the nucleotides dG has been substituted with a nucleotide dI is at least equal to two.

9. The array of at least two different probes as claimed in one of claims 1 to 8, characterized in that said receptor is the serotonin 5-HT_{2c} receptor (5-HT_{2c}-R) or the glutamate receptor B subunit (GluR-B).

10. The array of at least two different probes as claimed in one of claims 1 to 9, characterized in that said array consists of or comprises a set of thirty-two distinct probes for detecting and/or quantifying, in a sample, any target oligonucleotide derived from a fragment comprising the sequence SEQ ID No. 33 (5'-AUA CGU AAU CCU A-3') of the edited or unedited mRNA of 5-HT_{2c}-R, said array consisting of or comprising the following sets of probes:

- the set of thirty-two probes of sequence SEQ ID Nos. 1 to 32 below:

5'-CAATACGTAATCCTATT-3' (SEQ ID No. 1),
5'-CAITACGTAATCCTATT-3' (SEQ ID No. 2),
5'-CAATICGTAATCCTATT-3' (SEQ ID No. 3),
5'-CAATACGTAITCCTATT-3' (SEQ ID No. 4),
5'-CAATACGTAATCCTITT-3' (SEQ ID No. 5),
5'-CAATACGTIATCCTATT-3' (SEQ ID No. 6),
5'-CAITICGTAATCCTATT-3' (SEQ ID No. 7),
5'-CAITACGTAITCCTATT-3' (SEQ ID No. 8),
5'-CAITACGTAATCCTITT-3' (SEQ ID No. 9),
5'-CAITACGTIATCCTATT-3' (SEQ ID No. 10),
5'-CAATICGTAITCCTATT-3' (SEQ ID No. 11),
5'-CAATICGTAATCCTITT-3' (SEQ ID No. 12),
5'-CAATICGTIATCCTATT-3' (SEQ ID No. 13),
5'-CAATACGTAITCCTITT-3' (SEQ ID No. 14),
5'-CAATACGTIITCCTATT-3' (SEQ ID No. 15),
5'-CAATACGTIATCCTITT-3' (SEQ ID No. 16),
5'-CAITICGTAITCCTATT-3' (SEQ ID No. 17),
5'-CAITICGTAATCCTITT-3' (SEQ ID No. 18),
5'-CAITICGTIATCCTATT-3' (SEQ ID No. 19),
5'-CAITACGTAITCCTITT-3' (SEQ ID No. 20),
5'-CAITACGTIITCCTATT-3' (SEQ ID No. 21),
5'-CAITACGTIATCCTITT-3' (SEQ ID No. 22),
5'-CAATICGTAITCCTITT-3' (SEQ ID No. 23),

5'-CAATICGTIITCCTATT-3' (SEQ ID No. 24),
5'-CAATICGTIATCCTITT-3' (SEQ ID No. 25),
5'-CAATACGTIITCCTITT-3' (SEQ ID No. 26),
5'-CAITICGTAITCCTITT-3' (SEQ ID No. 27),
5'-CAITICGTIITCCTATT-3' (SEQ ID No. 28),
5'-CAITICGTIATCCTITT-3' (SEQ ID No. 29),
5'-CAITACGTIITCCTITT-3' (SEQ ID No. 30),
5'-CAATICGTIITCCTITT-3' (SEQ ID No. 31), and
5'-CAITICGTIITCCTITT-3'(SEQ ID No. 32); or

- the set of thirty-two probes of sequence comprising the sequences of the fragments from nucleotide 3 to nucleotide 15 of SEQ ID Nos. 1 to 32.

11. A biochip comprising an array of at least two different probes as claimed in one of claims 1 to 10, deposited on the same solid support.

12. The biochip as claimed in claim 11, characterized in that said solid support is chosen from solid supports made of glass, plastic, Nylon®, silicone, silicon or polysaccharides.

13. The biochip as claimed in claim 11 or 12, characterized in that said probes are attached to said solid support, preferably by covalent bonding.

14. A reactor comprising, in solution, an array of at least two different probes as claimed in one of claims 1 to 10.

15. A device, in particular a plate or a microplate, consisting of at least two containers, preferably two cupules, said device comprising an array of at least two different probes as claimed in one of claims 1 to 10, each of the containers containing one of said probes.

16. A kit of reagents for detecting, or qualitatively or quantitatively analyzing target nucleic acids in a sample, characterized in that it comprises an array of at least two different probes as claimed in one of claims 1 to 10, a biochip as claimed in one of claims 11 to 13, or a device as claimed in claim 15.

17. A method for detecting and/or quantifying target oligonucleotides in a sample, said target oligonucleotide being derived from an mRNA fragment encoding a membrane receptor from a mammalian cell, which may comprise at least one editing site in the sequence of this fragment, characterized in that it comprises the following steps:

a) depositing the sample containing said target oligonucleotides, the detection of whose presence is sought, on a biochip as claimed in one of claims 11 to 13, or in each of the containers of the device as claimed in claim 15, under the conditions for the specific hybridization of said target oligonucleotides with said probes;

b) where appropriate, rinsing the biochip obtained in step a) under the conditions for removing the nucleic acids of the sample that have not been captured by hybridization; and

c) detecting and/or quantifying the target oligonucleotides captured by specific hybridization at each of said probes.

18. The method for detecting and/or quantifying target oligonucleotides in a sample as claimed in claim 17, characterized in that said target oligonucleotide is derived from a fragment comprising the sequence SEQ ID No. 33 (5'-AUA CGU AAU CCU A-3') of the edited or unedited mRNA of 5-HT_{2C}-R.

19. A method for determining the percentage, in the same sample, of each of the edited and unedited forms of an mRNA fragment encoding a membrane receptor from a mammalian cell, which may comprise at least one editing site, relative to the total amount of the edited or unedited mRNA forms present in said same sample (called "editing rate"), characterized in that it comprises a method as claimed in claim 17 and in that, at the end of step c) of said method as claimed in claim 17, the ratio, expressed as a percentage, of the amount of oligonucleotides captured by a probe to the total amount of oligonucleotides captured by the set of probes is determined for each of said probes.

20. The method as claimed in claim 19, characterized in that said mRNA fragment encoding a membrane receptor which may comprise at least one editing site is the fragment comprising the sequence SEQ ID No. 33 (5'-AUA CGU AAU CCU A-3') of the edited or unedited mRNA of 5-HT_{2C}-R, and in that, in step a) of the method as claimed in claim 17, said biochip or the containers of said device comprise an array of probes as claimed in claim 10.

21. The method as claimed in one of claims 17 to 20, characterized in that the target oligonucleotides are antisense mRNAs or complementary DNAs of the fragments of said edited and unedited mRNA, and in that said probes are DNAs corresponding to the sequences of the fragment of said edited and unedited mRNA.

22. The method as claimed in one of claims 17 to 21, characterized in that said fragments from which the target oligonucleotides are derived are fragments of nucleic acids extracted from a biological sample from a mammal, including a human being.

23. The method as claimed in one of claims 17 to 22, characterized in that the target oligonucleotides are prelabeled with a label capable of producing, directly or indirectly, a detectable signal, preferably a fluorescent or radioactive signal.

24. The use of a biochip as claimed in one of claims 11 to 13, or of a device as claimed in claim 15, for determining the editing rate of an mRNA encoding a membrane receptor from a mammalian cell.

25. A method for selecting a compound capable of modulating the editing of an editing site located on a fragment of an mRNA encoding a membrane receptor present in a mammalian cell, said edited mRNA fragment having the sequence given the notation "E" and said unedited mRNA fragment having the sequence given the notation "UE", characterized in that it comprises the following steps:

A) bringing said compound to be evaluated into contact with a population of cells expressing the gene of said mRNA capable of being edited;

B) demonstrating the modulation or non-modulation of the editing of the editing site of said mRNA in said cell using a sample of target oligonucleotides derived from said mRNA fragment and obtained from a nucleic acid extract derived from said cells obtained in step A), by means of a method as claimed in claim 17 and in which method at least two of said probes are two DNAs, one corresponding to the DNA sequence of said fragment "E" and the other corresponding to the DNA sequence of said fragment "UE";

C) where appropriate, in that, in step c) of the method as claimed in claim 17, the detection and/or the quantification of the target oligonucleotides captured at each of said probes are compared with those obtained using a population of control cells; and

D) selecting this compound if it modulates the editing of said editing site.

26. A method for selecting compounds capable of modulating the editing rate of an mRNA fragment encoding a membrane receptor present in a mammalian cell, characterized in that it comprises the following steps:

A) bringing said compound to be evaluated into contact with a population of cells expressing the gene of said mRNA capable of being edited;

B) demonstrating the modulation or non-modulation of the editing rate of said mRNA fragment in said cell using a sample of target oligonucleotides derived from said mRNA fragment and obtained from a nucleic acid extract derived from said cells obtained in step A), by means of a method as claimed in claim 17;

C) determining, at the end of step c) of the method as claimed in claim 17 and for each of said probes, the editing rate corresponding to the ratio, expressed as a percentage, of the amount of oligonucleotides captured by a probe to the total amount of oligonucleotides captured by the set of probes;

D) where appropriate, in that the editing rate obtained is compared with that obtained for a population of control cells; and

E) selecting this compound if it modulates the editing rate of said mRNA fragment.

27. The method for selecting compounds capable of modulating the editing rate of an mRNA fragment as claimed in claim 26, said mRNA encoding the membrane

receptor 5-HT_{2C}-R, characterized in that said mRNA fragment comprises the sequences SEQ ID No. 33 (5'-AUA CGU AAU CCU A-3') of the 5-HT_{2C}-R mRNA and in that, in step B of said method, the demonstration of the modulation or non-modulation of the editing rate of said mRNA fragment is carried out by means of a method as claimed in claim 18 in which, in step a), said biochip or the containers of said device comprise an array of probes as claimed in claim 10;

C) determining, at the end of step c) of the method as claimed in claim 18 and for each of said probes, the editing rate corresponding to the ratio, expressed as a percentage, of the amount of oligonucleotides captured by a probe to the total amount of oligonucleotides captured by the set of probes;

D) where appropriate, in that the editing rate obtained is compared with that obtained for a population of control cells; and

E) selecting this compound if it modulates the editing rate of said mRNA fragment.

28. An SSCP method for obtaining, under given analytical conditions, the editing profile of an mRNA which may be edited, using a specific tissue sample or using a sample of a population of eukaryotic cells, characterized in that it comprises the following steps:

a) extraction of the total RNAs of said sample, followed, where appropriate, by purification of the mRNAs;

b) reverse transcription of the RNAs extracted in step a) and synthesis of the double-stranded DNA;

c) PCR amplification of the DNAs obtained in step b) using a pair of primers specific for said mRNA which may be edited, this pair of primers being chosen so as to be able to amplify all the editing forms potentially present in the RNA extract, these primers being labeled with fluorophores;

d) where appropriate, purification of the PCR products obtained in step c);

e) where appropriate, quantification of the PCR products obtained in step d);

f) dissociation of the double-stranded DNAs to single-stranded DNAs, in particular by heating followed by abrupt cooling;

g) separation of the single-stranded DNAs by capillary electrophoresis; and

h) obtaining of the editing profile by reading of the fluorescence and, where appropriate, acquisition of the profile data by means of the exploitation system associated with the fluorescence reader.

29. The SSCP method as claimed in claim 28, characterized in that the pair of primers used in step c) is chosen such that the PCR products obtained are at least 100 bases in length.

30. The SSCP method as claimed in claim 28 or 29, characterized in that said mRNA which may be edited is that of a membrane receptor, in particular 5-HT_{2C}-R, or that of the glutamate receptor B subunit (GluR-B).

31. The SSCP method as claimed in claim 30, characterized in that said mRNA which may be edited is that of 5-HT_{2C}-R or that of the glutamate receptor B subunit (GluR-B).

32. The SSCP method as claimed in claims 28 to 31, characterized in that said mRNA which may be edited is that of 5-HT_{2C}-R, and the pair of primers is the following pair of primers, preferably labeled with fluorophores:

PCR9 TGTCCCTAGCCATTGCTGATATGCT (SEQ ID No. 36); and

PCR10 GCAATCTTCATGATGGCCTTAGTCCG (SEQ ID No. 37).

33. An SSCP method for obtaining, under given analytical conditions, the editing profile and the editing rate of an mRNA which may be edited, using a specific tissue sample or using a sample of a population of eukaryotic cells, characterized in that it comprises the following steps:

a) obtaining the editing profile by means of the SSCP method as claimed in one of claims 28 to 32;

b) comparing the profile obtained in step a) with standard profiles corresponding to:

- characteristic profiles obtained, under these given conditions, for each of the edited (or unedited) separate forms of said mRNA; and/or
- characteristic profiles of known qualitative and/or quantitative mixtures of each of these edited or unedited forms, obtained under these given conditions; and/or
- known editing profiles, under these same given conditions, of this same mRNA for normal patients or patients presenting confirmed pathologies, for mRNA extracts of said specific tissues, or else for said population of eukaryotic cells;

c) selecting the known editing profile corresponding to the editing profile obtained in step a); and

d) associating the editing rate of the profile selected in step c) with the editing profile obtained in step a).

34. A method for selecting a compound capable of modulating the editing rate and/or the editing profile of an mRNA capable of being edited in a specific tissue or a population of eukaryotic cells expressing the gene of said mRNA, in particular from a mammal, such as human or mouse, characterized in that it comprises the following steps:

a) bringing said compound to be evaluated into contact, *in vivo* or *in cellulo*, with said specific tissue or said population of eukaryotic cells;

b) obtaining the editing profile by means of the SSCP method as claimed in claims 28 to 33, under given analytical conditions;

c) comparing the profile obtained in step b) with:

- either standard profiles corresponding to known editing profiles of this same mRNA, for the same specific tissue or the same population of eukaryotic cells, under the same given analytical conditions,

- or an editing profile determined in parallel and obtained for the same control specific tissue or the same population of control eukaryotic cells that have not been brought into contact with the compound to be evaluated; and

d) selecting said compound to be evaluated if the editing profiles compared in step c) are significantly different from one another.

35. A method for selecting a compound capable of preventing and/or treating, in a patient, a pathology associated, at least in part, with the editing of an mRNA capable of being edited, characterized in that it comprises the following steps:

a) bringing said compound to be evaluated into contact, *in vivo* or *in cellulo*, with a specific tissue or a population of eukaryotic cells expressing the gene of said mRNA capable of being edited, said specific tissue or said population of eukaryotic cells exhibiting, before being brought into contact with the compound to be tested, an editing profile of said mRNA characteristic of the associated pathology, under given analytical conditions;

b) obtaining the editing profile by means of the SSCP method as claimed in claims 28 to 33, under these given analytical conditions;

c) comparing the profile obtained in step b) with:

α) a standard profile corresponding to a known editing profile of this same mRNA, for the same specific tissue or for the same population of cells, under the same given analytical conditions, this editing profile being representative of a normal patient or a patient not presenting said associated pathology; and, where appropriate, with:

β) an editing profile obtained for the same control specific tissue or for the same population of control cells that have not been brought into contact with the compound to be evaluated, under the same given analytical conditions; and

d) selecting said compound to be evaluated if the editing profiles compared in step c) show that the one obtained in step b) is significantly identical to the one in step c)α), and, where appropriate, confirming this selection if the profile obtained in step b) is significantly different from the one in step c)β).

36. A method for selecting a compound capable of preventing and/or treating, in a patient, a pathology associated, at least in part, with the editing or nonediting of an

mRNA capable of being edited, with the same therapeutic mechanism or effectiveness as a compound known to modulate the editing profile of said RNA and known to prevent and/or treat, in a patient, the same associated pathology, characterized in that it comprises the following steps:

a) bringing said compound to be evaluated into contact, *in vivo* or *in cellulo*, with a specific tissue or a population of eukaryotic cells expressing the gene of said mRNA capable of being edited, said specific tissue or said population of eukaryotic cells exhibiting, before being brought into contact with the compound to be tested, an editing profile of said mRNA characteristic of the associated pathology, under given analytical conditions;

b) obtaining the editing profile by means of the SSCP method as claimed in claims 28 to 33, under these given analytical conditions;

c) comparing the profile obtained in step b) with:

α) a standard profile corresponding to a known editing profile of this same mRNA, for the same specific tissue or for the same population of cells having been brought into contact, *in vivo* or *in cellulo*, with said compound known to modulate the editing profile of said RNA, under the same given analytical conditions, and known to prevent and/or treat, in a patient, the same associated pathology; and, where appropriate, with:

β) an editing profile obtained for the same control specific tissue or for the same population of control cells that have not been brought into contact with the compound to be evaluated, under the same given analytical conditions; and

d) selecting said compound to be evaluated if the editing profiles compared in step c) show that the one obtained in step b) is significantly identical to the one in step c)α), and, where appropriate, confirming this selection if the profile obtained in step b) is significantly different from the one in step c)β).

37. A method for diagnosing, where appropriate for predicting, a disease associated, at least in part, with an mRNA capable of being edited, using a tissue or cell sample taken from a patient to be tested, characterized in that it comprises the following steps:

a) obtaining the editing profile of said mRNA by means of the SSCP method as claimed in claims 28 to 33, under given analytical conditions;

b) comparing the profile obtained in step a) with standard profiles corresponding to known editing profiles of this same mRNA for normal patients or patients exhibiting confirmed pathologies, for mRNA extracts of the same tissue or of

the same cells, under these same given conditions, or else for cells derived from cell lines; and

c) selecting the known editing profile corresponding to the editing profile obtained in step a); and

d) associating the diagnosis related to the profile selected in step c), with the patient tested.

38. The method for selecting a compound capable of modulating the editing rate of the RNA fragment comprising the sequence SEQ ID No. 33 (5'-AUA CGU AAU CCU A-3') of the 5-HT_{2C}-R mRNA, as claimed in claim 27, or the method for selecting a compound capable of modulating the editing rate and/or the editing profile of the 5-HT_{2C}-R mRNA, as claimed in claim 34, characterized in that, in step E) of the method as claimed in claim 27, or in step d) of the method as claimed in claim 34, the compound is selected if it decreases the editing rate of an editing site of said RNA fragment, which editing site, when it is edited, modifies the amino acid sequence of 5-HT_{2C}-R originating from the translation of the unedited mRNA.

39. The method for selecting a compound capable of modulating the editing rate of the RNA fragment comprising the sequence SEQ ID No. 33 (5'-AUA CGU AAU CCU A-3') of the 5-HT_{2C}-R mRNA, as claimed in claim 27, or the method for selecting a compound capable of modulating the editing rate and/or the editing profile of an mRNA encoding 5-HT_{2C}-R, as claimed in claim 34, characterized in that, in step E) of the method as claimed in claim 27, or in step d) of the method as claimed in claim 34, the compound is selected if it increases the editing rate of an editing site of said RNA fragment, which editing site, when it is edited, modifies the amino acid sequence of 5-HT_{2C}-R originating from the translation of the unedited mRNA.